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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/06/2003

Antonio Arevalo Reyes

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EXAMINER

MYERS, CARLA J

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 07/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/680,341	REYES ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) ☒ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) ☐ Notice of Informal Patent Application (PTO-152) |
| 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/6/03</u> . | 6) ☐ Other: _____ |

DETAILED ACTION

Specification

1. The specification is objected to over the following informalities:

In claim 2, step b) "primer extension products; from" should read "primer extension products from".

In claim 7, a period should be inserted at the end of the claim.

Priority

2. It is noted that the present claims are not entitled to priority to applications 08/826,532 or 08/095,442. While the '532 and '442 applications disclose the amplification of "nucleic acids" using primers containing a non-replicable element, these applications do not specifically disclose methods for synthesizing a cDNA from an RNA molecule using a primer containing a non-replicable element.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-31 are indefinite because the claims do not set forth a clear relationship between the steps of annealing the first and second primers and the steps of generating the first and second strand cDNA products. That is, it is unclear as to whether, e.g., the

Art Unit: 1634

first strand cDNA product is produced by annealing a first primer to an RNA molecule and extending the first primer to form a first strand cDNA product, or if the first strand cDNA product is produced in a separate process in which a different, unspecified primer is annealed to a template and extended to form a first strand cDNA product.

Claims 1-31 are also indefinite because they refer to both first and second strand cDNAs and to first and second strand cDNA products. However, it is unclear as to whether the first and second cDNAs are the same as or distinct from the first and second strand cDNA products. It is also unclear as to what is intended to be the relationship between the cDNA molecule and the first and second strand cDNAs and the first and second strand cDNA products.

Claims 1-15 are indefinite over the recitation in claim 1 step b) of "its template" because this phrase lacks proper antecedent basis since the claim does not previously refer to a template.

Claims 2-15 and 17-30 are indefinite over the recitation of "said strands" because this phrase lacks proper antecedent basis. While the claims previously refer to first and second strand cDNA and first and second strand cDNA products, the claims do not previously refer more generally to "strands." Thereby, it is unclear as to whether "said strands" refers to the first and second strand cDNA or first and second strand cDNA products or to some other unspecified strands.

Claims 2, 6-15, 17, and 21-30 are indefinite over the recitations of "the second amplification primer" and "their respective templates" because these phrases lack proper antecedent basis.

Art Unit: 1634

Claims 2, 6-15, 17, and 21-30 are indefinite over the recitation at step d) of “the second generation amplification primers” because this phrase lacks proper antecedent basis.

Claims 2-4, 6-15, are indefinite over the recitations at step d) of “the binding site” and “the nucleic acid sequence of said first generation amplification primer” because these phrases lack proper antecedent basis.

Claims 2-4, 6-15 are indefinite over the recitation of “insufficient portion of the binding site” because the specification does not provide a clear definition for this phrase and there is no art recognized definition for this phrase. The claims do not clearly set forth the criteria for determining whether a portion is “insufficient” – i.e., the claims do not state what the portion is to be insufficient for. For example, it is unclear as to whether an insufficient portion refers to a nucleic acid sequence that does not permit the second generation primers to bind and does not serve as a site for primer-dependent DNA synthesis for the second generation primers or if an “insufficient portion” is a nucleic acid that may be missing one or two terminal nucleotides but which still permits primer binding and extension.

Claims 2-4, 6-15, 17-19, and 21-31 are indefinite over the recitation of **“the sequence of the nucleic acid sequence** of said first generation amplification primer” because this phrase lacks proper antecedent basis.

Claims 4, 6-15, 19 and 21-30 are indefinite over the recitation at step c) of “said sequence of said first and second cDNA strands” because this phrase lacks proper

Art Unit: 1634

antecedent basis. While the claim previously refers sequences of the first and second cDNA strands.

Claims 4-15, and 19-30 are indefinite over the recitation of “the next prior generation primer extension products” because this phrase lacks proper antecedent basis and it is unclear as to what is intended to be encompassed by this phrase.

Claims 4-15, and 19-30 are indefinite over the recitation of “**the position** of said non-replicable element...” because this phrase lacks proper antecedent basis

Claims 5, 6-15, 20, and 21-30 are indefinite over the recitation at step b) of “the sequence of interest” because this phrase lacks proper antecedent basis.

Claims 5-15 and 20-30 are indefinite over the recitations of “its respective complementary sites” and “their respective templates” because these phrases lack proper antecedent basis.

Claims 11 and 26 are indefinite over the recitation of “said first generation primer extension product” because this phrase lacks proper antecedent basis.

Claims 11 and 26 are indefinite over the recitation of “said product” because it is not clear as to whether this recitation refers to the first and second cDNA products or to the first generation primer extension product.

Claims 14, 15, 29 and 30 are indefinite over the recitations of “is a residue of” because it is unclear as to what is meant by a residue of the stated compounds. For instance, it is not clear as to whether the claims intend to refer to non-replicable elements that contain just one molecule of 1,3-propane diol or 1,4-anhydro-2-deoxy-D-

Art Unit: 1634

ribitol (e.g., one carbon residue) or if the claims intend to refer to non-replicable elements which comprise 1,3-propane diol or 1,4-anhydro-2-deoxy-D-ribitol.

Claims 17-30 are indefinite over the recitation of “generating a first strand cDNA **product** according to the process of claim 16” because this phrase lacks proper antecedent basis since claim 16 is drawn to a method for generating a cDNA molecule. While claim 16 does include a step of producing a first strand cDNA product, it is improper for a dependent claim to refer back to and claim only a portion of the steps of a claim from which it depends.

Claims 18-30 are indefinite over the recitation of “the first and **second cDNA strands**” because this phrase lacks proper antecedent basis since the claims do not previously refer to a second cDNA strand.

Claims 23-26 are indefinite and vague over the recitation of “said primer of step (b) of the dependent claim” because this phrase lacks proper antecedent basis and it is unclear as to what constitutes “the dependent claim.”

Claim 31 is indefinite over the recitation of “its template” because this phrase lacks proper antecedent basis.

Claim 31 is indefinite over the recitation of “strands as templates” because it is unclear as to what constitutes the strands. While the claim previously refers to first and second strand cDNA and first and second strand cDNA products, the claim does not previously refer more generally to “strands.” Thereby, it is unclear as to whether “strands” refers to the first and second strand cDNA or first and second strand cDNA products or to some other unspecified strands.

Art Unit: 1634

Claim 31 is indefinite over the recitation of "said amplification primer for a first strand cDNA" because this phrase lacks proper antecedent basis. While the claim previously refers to "at least one amplification primer" the claim does not previously refer to an "amplification primer for a first strand cDNA."

Claim 31 is indefinite over the recitation at step h) of "said second generation amplification primers" because this phrase lacks proper antecedent basis.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,335,184.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of '184 are both inclusive of

Art Unit: 1634

methods for generating a cDNA molecule from an RNA molecule wherein the methods comprise the steps of annealing a first primer containing a non-replicable element to an RNA molecule, extending the first primer to form a first strand cDNA, separating the first strand cDNA from the RNA, annealing a second primer to the cDNA, extending the first strand cDNA to form a second strand cDNA product and then combining the resulting cDNA with amplification primers containing non-replicable elements and/or cleavable elements to form second generation amplification products containing a region that is not sufficient for the binding of the amplification primers. While the claims of '184 recite the amplification of any nucleic acid of sequence, the recitation of the genus of any nucleic acid encompasses the presently claimed nucleic acid species of RNA.

5. Claims 1-3, 6-18 and 21-31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-45 of U.S. Patent No. 6,027,923 in view of Mullis (US Patent No. 4965188).

The present claims and the claims of '923 are both inclusive of methods for performing primer extension and amplification reactions wherein the methods comprise the steps of annealing a first primer containing a non-replicable element to a template, extending the first primer to form a first strand, separating the first strand from the template, annealing a second primer to the first strand, extending the primer to form a second strand, and then combining the resulting strands with amplification primers containing non-replicable elements and/or cleavable elements to form second generation amplification products containing a region that is not sufficient for the binding of the amplification primers. While the claims of '923 recite the amplification of any

Art Unit: 1634

nucleic acid of sequence, the claims of '923 do not specifically recite the use of RNA templates.

However, Mullis (see, e.g., Example IV) teaches methods for synthesizing cDNA using a RNA template and then amplifying the resulting cDNA by PCR to generate amplification products.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of the claims of '923 so as to have used RNA in place of cDNA as a template in order to have provided a fast and effective means for linearly amplifying a RNA molecule of interest.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6, 7, 12, 13, 16, 21, 22, 27, 28 and 31 are rejected under 35

U.S.C. 102(e) as being anticipated by Newton et al (U.S. Patent No. 5,525,494).

Newton (see, for example, col. 2-3) teaches a method for amplifying a target nucleic acid wherein the method comprises contacting a sample nucleic acid, together or sequentially, with a first primer comprising a target binding region and a polynucleotide tail and with an amplification primer comprising a target binding region

Art Unit: 1634

and a polynucleotide tail, in the presence of a polymerization agent under conditions in which the first primer and amplification primer anneal to the target nucleic acid and wherein the first primer and the amplification primer are extended to generate an amplification product. The first primer and the amplification primer each contain a polymerization blocking moiety positioned between the target binding region and the tail (see col. 2 and 3). In particular, "the first primer may be subjected to primer extension whereby a first primer extension product is synthesized based on the target nucleotide sequence as template, and after denaturation of the first primer extension product from its template and hybridization of the amplification primer to the desired portion of the first primer extension product, primer extension may be effected to form an amplification primer extension product, the presence of the first primer in the first primer extension product being effective to inhibit formation of a sequence complementary to the polynucleotide tail in the amplification primer extension product" (see col. 2, lines 36-48). Similarly, the presence of the amplification primer in the amplification primer extension product is effective to inhibit the formation of a sequence complementary to the polynucleotide tail of the primer extension product. Accordingly, Newton teaches amplification methods utilizing a first and second primer comprising a "non-replicable element". Newton teaches that the target sequence may be RNA or DNA (col. 6, lines 20-24) and teaches that the agent for polymerization may be any suitable DNA polymerase or reverse transcriptase (see col. 6, lines 44-51). The method of annealing primers to the template and separating the primer extension products from their templates may be repeated as many times as necessary to obtained the desired level of

Art Unit: 1634

sequence amplification (col. 2). Thereby, Newton teaches that the amplification method is one for synthesizing cDNA from an RNA template and for further amplifying cDNA amplification products.

Regarding claims 6 and 21, Newton teaches that the blocking moiety is positioned between the target specific binding region and the primer tail, and thereby is not located at a terminal residue of the primer (col. 2).

Regarding claims 7 and 22, since the "cleavable element" is optional, the recitations in these claims are not considered to further limit the method of claims 1 and 16.

Regarding claims 12, 13, 27 and 28, Newton (col. 9) teaches that the polymerization blocking moiety may be a deoxy ribofuranosyl naphthalene or ribofuranosyl naphthalene moiety, which are considered to be derivatives of a deoxyribonucleotide and derivatives of a ribonucleotide.

Regarding claims 31, since the primer contains a tail that is not complementary to the target sequence, such a primer is considered to meet the claim limitations of a primer containing "no more than an insufficient portion of the binding site."

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 6, 7, 12-14, 16, 21, 22, 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over McDonough et al (U.S. Patent No. 5,766,849).

McDonough (col. 7-8) teaches a method for synthesizing cDNA comprising:
a) annealing a primer containing a blocking agent to a RNA molecule; b) annealing a primer without a blocking agent to a RNA molecule, and extending the primer to form a first cDNA product; c) separating the first cDNA products from templates to form single stranded molecules; d) annealing a second primer containing a blocking agent to the single stranded molecules of c); e) annealing a second primer not containing a blocking agent to the single stranded molecules of c), and extending the second primer to produce second strand cDNA products.

It is noted that the present claims encompass methods in which the first strand cDNA product and second strand cDNA product are generated using any primer. In the method of McDonough, a mixture of primers are used containing both 3' blocked primers and unblocked primers. The blocked primers are considered to meet the claim limitations of "primers containing a non-replicable element" because the primers contain a moiety that blocks primer extension (see col. 8, lines 36-50) and thereby prevents replication of the entire sequence of the primer. Accordingly, in the method of McDonough, steps a) and d) of claim 1 and step a) of claim 16 are accomplished using the primers containing a blocking agent, while steps b) and e) of claim 1 and step b) of claim 16 are accomplished using the primer that does not contain a blocking moiety.

Regarding claims 6 and 21, McDonough teaches that the blocking agent may be 3 bases from the 3' terminus of the primer.

Art Unit: 1634

Regarding claims 7 and 22, since the “cleavable element” is optional, the recitations in these claims are not considered to further limit the method of claims 1 and 16.

Regarding claims 12, 13, 27 and 28, McDonough (col. 5, lines 9-23) teaches that the blocking agent is a ribonucleotide or a 3'-2' dideoxy nucleotide (i.e., a “derivative of a deoxyribonucleotide”).

Regarding claims 14 and 29, McDonough teaches that the blocking moiety may contain alkane diol modifications. In particular, McDonough teaches that the alkane diol blocking moiety may be a propane (i.e., “N=3”; figure 1) and teaches attachment of propane diol to a phosphate of a nucleotide via the phosphate group. Accordingly, McDonough teaches a primer containing a non-replicable element that is “a residue of 1, 3-propane diol.”

8. Claims 14 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Newton in view of McDonough.

The teachings of Newton are presented above. In particular, Newton teaches that any moiety which blocks polymerization may be incorporated into the primer as the blocking moiety (see, e.g., col. 8-9). Newton does not specifically exemplify primers containing 1, 3-propane diol.

However, McDonough (col. 5 and Figure 1) teaches primers containing blocking moieties, such as alkane diols which inhibit primer extension and replication reactions. In particular, McDonough teaches that the alkane diol may be a propane (i.e., “N=3”;

Art Unit: 1634

figure 1) and teaches attachment of propane diol to a phosphate of a nucleotide via the phosphate group (i.e., "a residue of 1,3-propane diol").

In view of the teachings of McDonough, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have incorporated a 1, 3-alkane diol into the primer of Newton in order to have provided an equally effective blocking moiety for inhibiting primer extension and replication.

8. Claims 15 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Newton in view of in view of Smith et al (US Patent No. 5,708,154).

The teachings of Newton are presented above. In particular, Newton teaches that any moiety which blocks polymerization may be incorporated into the primer as the blocking moiety (see, e.g., col. 8-9). However, Newton does not specifically exemplify primers containing 1, 4-anhydro-2-deoxy-D-ribitol.

However, Smith teaches the incorporation of abasic residues into nucleic acids as a means for inhibiting polymerization reactions (see col. 2 and 4). In particular, Smith teaches that reverse transcriptase reactions are inhibited when a 1, 4-anhydro-2-deoxy-D-ribitol moiety is incorporated into the nucleic acid (col. 4).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Newton so as to have incorporated a 1, 4-anhydro-2-deoxy-D-ribitol moiety into the primer because this would have provided an equally effective blocking moiety for inhibiting primer extension and replication.

Art Unit: 1634

9. Claims 15 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over McDonough in view of Smith.

The teachings of McDonough are presented above. In particular, McDonough teaches that any moiety which blocks polymerization may be incorporated into the primer as the blocking moiety (see, e.g., col. 5). For instance, the blocking moiety may be a 3' alkane diol (see Figure 1). McDonough does not specifically exemplify primers containing 1, 4-anhydro-2-deoxy-D-ribitol.

However, Smith teaches the incorporation of abasic residues into nucleic acids as a means for inhibiting polymerization reactions (see col. 2 and 4). In particular, Smith teaches that reverse transcriptase reactions are inhibited when a 1, 4-anhydro-2-deoxy-D-ribitol moiety is incorporated into the nucleic acid (col. 4).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of McDonough so as to have incorporated a 1, 4-anhydro-2-deoxy-D-ribitol moiety into the primer because this would have provided an equally effective blocking moiety for inhibiting primer extension.

10. Claims 1-3, 6-10, 12-18 and 21-25, and 27-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace (WO 95/03432; cited in the IDS) in view of Mullis.

Wallace teaches methods for performing primer extension and amplification reactions wherein the methods comprise the steps of annealing a first primer containing a non-replicable element to a template, extending the first primer to form a first strand, separating the first strand from the template, annealing a second primer to the first strand, extending the primer to form a second strand, and then combining the resulting

Art Unit: 1634

strands with amplification primers containing non-replicable elements and/or cleavable elements to form second generation amplification products containing a region that is not sufficient for the binding of the amplification primers. While Wallace teaches that the method may be applied to a nucleic acid, Wallace does not specifically exemplify methods in which an RNA template is used for the primer extension reaction.

However, Mullis (see, e.g., Example IV) teaches methods for synthesizing cDNA using a RNA template and then amplifying the resulting cDNA by PCR to generate amplification products.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Wallace so as to have used RNA in place of cDNA as a template in order to have provided a fast and effective means for linearly amplifying an RNA molecule of interest.

Regarding claims 2, 3, 17 and 18, Wallace teaches treating first generation primer extension products with primers to generate second generation primer extension products and teaches that the second generation amplification extension products accumulate in a linear fashion (pages 5 and 6).

Regarding claims 6 and 21, Wallace teaches that the blocking element is not at the 3' terminus of the primer.

Regarding claims 7 and 22, since the "cleavable element" is optional, the recitations in these claims are not considered to further limit the method of claims 1 and 16.

Regarding claims 12-16 and 27-30, Wallace (e.g, page 17) teaches that the blocking agent is a ribonucleotide (i.e., a derivative of a deoxyribonucleotide), or is preferably a 1,3- propane diol or a 1,4-anhydro-2-deoxy-D-ribitol moiety.

11. Claims 1-3, 6-18 and 21-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace (U.S. Patent No. 6,027,923) in view of Mullis.

Wallace teaches methods for performing primer extension and amplification reactions wherein the methods comprise the steps of annealing a first primer containing a non-replicable element to a template, extending the first primer to form a first strand, separating the first strand from the template, annealing a second primer to the first strand, extending the primer to form a second strand, and then combining the resulting strands with amplification primers containing non-replicable elements and/or cleavable elements to form second generation amplification products containing a region that is not sufficient for the binding of the amplification primers. While Wallace teaches that the method may be applied to a nucleic acid, Wallace does not specifically exemplify methods in which an RNA template is used for the primer extension reaction.

However, Mullis (see, e.g., Example IV) teaches methods for synthesizing cDNA using a RNA template and then amplifying the resulting cDNA by PCR to generate amplification products.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Wallace so as to have used RNA in place of cDNA as a template in order to have provided a fast and effective means for linearly amplifying an RNA molecule of interest.

Art Unit: 1634

Regarding claims 2, 3, 17 and 18, Wallace teaches treating first generation primer extension products with primers to generate second generation primer extension products and teaches that the second generation amplification extension products accumulate in a linear fashion (pages 5 and 6).

Regarding claims 6 and 21, Wallace teaches that the blocking element is not at the 3' terminus of the primer.

Regarding claims 7 and 22, Wallace (col. 9) teaches the use of primers containing a cleavable element, such as a ribonucleoside, that is not at the 3' terminus.

Regarding claims 11 and 26, Wallace (col. 9-10) teaches cleaving the primer extension product with a ribonuclease.

Regarding claims 12-16 and 27-30, Wallace (e.g., col. 9) teaches that the blocking agent is a ribonucleotide (i.e., a derivative of a deoxyribonucleotide), or is preferably a 1,3- propane diol or a 1,4-anhydro-2-deoxy-D-ribitol moiety.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)-272-0735.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Art Unit: 1634

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers


CARLA J. MYERS
PRIMARY EXAMINER